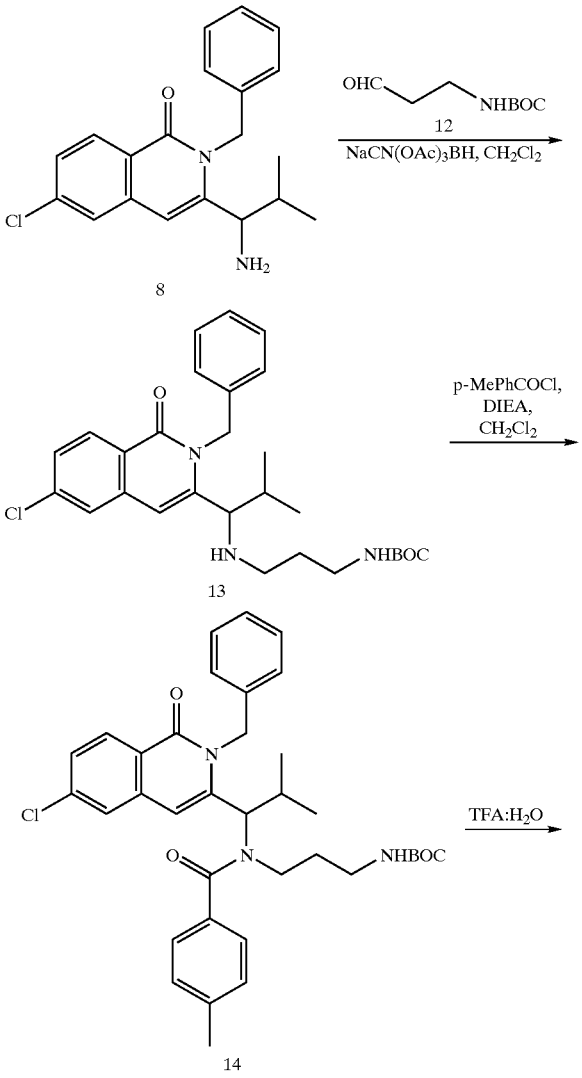
[0408] Isoquinolone 8 (131 mg, 0.34 mmol), aldehyde 9 (115 mg, 0.56 mmol), $Na(OAc)_3BH$ (291 mg, 1.38 mmol), and CH_2Cl_2 (1.1 mL) was maintained at 23° C. for 3 h. The reaction mixture was diluted with EtOAc (20 mL) and washed with 1 N NaOH (5 mL) and brine (5 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. The resulting residue was purified by flash column chromatography (3:1 hexanes:EtOAc) to yield 150 mg (85%) of 10.

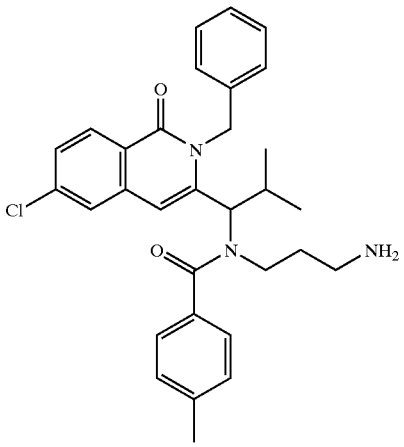
[0409] A solution of isoquinolone 10 (143 mg, 0.28 mmol), $POCl_3$ (0.45 mL, 4.8 mmol), and PhMe (T4 mL) was heated to 110° C. After 6 h, the reaction mixture was diluted with EtOAc (40 mL) and washed with 1 N NaOH (20 mL) and brine (10 mL) The organic layer was dried ($MgSO_4$), filtered, and concentrated. The resulting residue was purified by flash column chromatography (20:1 $CHCl_3$:MeOH) to yield 99 mg (70%) of 11 as a white solid.

Example 2

[0410] Synthesis of Compounds



-continued



[0411] Isoquinolone 8 (515 mg, 1.47 mmol), aldehyde 12 (255 mg, 1.47 mmol), $NaCN(OAc)_3BH$ (420 mg, 1.98 mmol), and CH_2Cl_2 (4.1 mL) was maintained at 23° C. for 2 h. An additional portion of 12 (225 mg, 1.30 mmol) in CH_2Cl_2 (0.6 mL) was then added. After an additional 3 h, the reaction mixture was diluted with EtOAc (20 mL) and washed with 1 N NaOH (5 mL) and brine (5 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. The resulting residue was purified by flash column chromatography (3:1 hexanes:EtOAc; 1:1 hexanes:EtOAc) to yield 630 mg (86%) of 13.

[0412] To a solution of isoquinolone 13 (85 mg, 0.17 mmol), diisoproylethylamine (DIEA, 0.12 mL, 0.68 mmol), and CH_2Cl_2 (0.6 mL) at 23° C. was added p-toluoyl chloride (45 μL, 0.34 mmol). After 4 h, the reaction mixture was diluted with EtOAc (20 mL) and washed with saturated aqueous $NaHCO_3$ (5 mL) and brine (5 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated. The resulting residue was purified by flash column chromatography (3:1 hexanes:EtOAc) to yield 83 mg (80%) of 14.

[0413] Isoquinolone 14 (80 mg, 0.13 mmol) and TFA:H_2O (97.5:2.5, 2 mL) was maintained at 23° C. for Th. The reaction mixture was concentrated. The residue was dissolved in EtOAc (20 mL) and washed with 1 N NaOH (5 mL) and brine (5 mL). The organic layer was dried ($MgSO_4$), filtered, and concentrated to provide 65 mg (98%) of 15 as a white solid which was deemed >95% pure by ^1H NMR and LCMS analysis.

Example 3

[0414] Using the methods of the invention as exemplified in Examples 1 and 2 above, the following compounds were prepared: